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EXAMINER

ZISKA,S

18M2/0104

ART UNIT

PAPER NUMBER

1804

6

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1804

DATE MAILED:

01/04/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

01/04/96

 This application has been examined Responsive to communication filed on 3/13/95 This action is made final.A shortened statutory period for response to this action is set to expire 4 months (3) month(s), 30 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. Notice of References Cited by Examiner, PTO-892.
2. Notice of Draftsman's Patent Drawing Review, PTO-948.
3. Notice of Art Cited by Applicant, PTO-1449.
4. Notice of Informal Patent Application, PTO-152.
5. Information on How to Effect Drawing Changes, PTO-1474.
6.

Part II SUMMARY OF ACTION

1. Claims 1 - 10 are pending in the application.

Of the above, claims _____ are withdrawn from consideration.

2. Claims _____ have been cancelled.3. Claims _____ are allowed.4. Claims 1 - 10 are rejected.5. Claims _____ are objected to.6. Claims _____ are subject to restriction or election requirement.7. This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.8. Formal drawings are required in response to this Office action.9. The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are acceptable; not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).10. The proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been approved by the examiner; disapproved by the examiner (see explanation).11. The proposed drawing correction, filed _____, has been approved; disapproved (see explanation).12. Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has been received not been received been filed in parent application, serial no. _____; filed on _____.13. Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1835 C.D. 11; 453 O.G. 213.14. Other

Art Unit: 1804

This application should be reviewed for errors.

Claims 1-10 are active and examined in this Office Action.

35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 1-10 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 17, 18, 20 and 85-94 of copending application Serial No. 08/270,412; claims 1-29 of copending application Serial No. 08/376,062 and claims 1-17 of copending application Serial No. 08/359,945. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed subject matter overlaps. The claims are drawn to method of regulating the proliferation of multipotent neural stem cells and their progeny using growth factors.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The obviousness-type double patenting rejection is a judicially established doctrine based upon public policy and is primarily intended to prevent prolongation of the patent term by prohibiting claims in a second patent not patentably distinct from claims in a first patent. *In re Vogel*, 164 USPQ 619 (CCPA 1970). A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) would overcome an actual or provisional rejection on this ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. § 1.78(d).

Claims 1-10 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "and/or" is vague and

Art Unit: 1804

unclear because either one or two different factors may be required and if applicants wish to claim a single factor that has both activities of regulating proliferation and inducing proliferation simultaneously, then such should be set apart as an independent claim.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 1-10 are rejected under 35 U.S.C. § 103 as being unpatentable over Boss taken with Anchan, Lin, Ferrari and Morshead. Boss discloses a method of a method for the proliferation of neuron progenitor cells. Boss discloses (column

Art Unit: 1804

3, "Summary") depending on the culture conditions and period, the progenitor cells differentiate either in vitro or in vivo; that the culture can be progenitor cells or aggregates of progenitor cells in a culture medium, or single or aggregated neuron progenitors cells on or dispersed in a substrate matrix; that most preferably the cultures are suspension cultures in which the progenitor cells grow as aggregates. Boss further discloses that the method comprises culturing the neuron progenitor cells in an initial culture medium which selects for a novel cell culture containing neuron progenitor cells (adaptive period) and growing the cells for a period of time (growth period) in a second medium. Boss discloses that the progenitor cells can be induced to differentiate in vitro by addition of a differentiation agent. Boss discloses that subculture is synonymous with "passage". Boss discloses that the obtained tissue is from human or porcine sources. Boss discloses the preparation of monolayer and suspension cultures from the dissociated cells (column 5); that the aggregate size is controlled by the culture conditions. Boss discloses that his cell population contains neural stem cells since (column 6) "... cells migrating from these (3-D) structures and form typical two dimensional monolayers in which differentiating neurons and glial cells can be observed. Boss discloses that (column 7) the cultures are initially grown in a first culture medium which promotes the survival of neuron progenitor cells which are capable of proliferating in a serum free-defined medium and that the initial culture medium can be supplemented with hormone and growth factors. Boss discloses passaging the cells (column 12) followed by plating on a fixed substrate, poly-L-ornithine, or alternatively reculturing in aggregates. Boss differs from the claims in that the reference fails to disclose culturing the cells in a culture medium containing at least one proliferative factor and induces stem

Art Unit: 1804

cell proliferation and a regulatory factor that regulates proliferation. However, the secondary references, Anchan, Morhead, Lin and Ferrari, cure the deficiency. Anchan discloses a method for the in vitro proliferation of neural stem cells comprising dissociation of rat neural tissue containing at least one multipotent stem cell capable of producing progeny capable of differentiating into neurons and glial cells. See page 923, column 2, "Results". Anchan discloses dissociating the retina to obtain a single cell suspension and culturing the cells in the presence of either EGF or TGF-alpha. Ferrari discloses that bFGF promotes survival and development of neurons in culture. Morshead discloses that the adult brain contains cells capable of dividing in a stem cell mode and it would have been obvious to one of ordinary skill to modify the method of Boss by using cells derived from adult tissue. Ferrari discloses GDNF, a neurotrophic factor capable of preventing degeneration of dopaminergic neurons.

It would have been obvious to one of ordinary skill to modify the method of Boss by adding other growth factors such as EGF, GDNF or bFGF in view of the teachings of Boss that other growth factors may be added and in view of the teachings of Boss that cells induced to express dopamine or neurotransmitters may be transplanted into a patient in need thereof. The use of heparin sulfate is obvious over the use of other growth factors since the specification discloses that heparin sulfate promotes binding of bFGF, for example, to its cell surface receptor.

Accordingly, the modification of the method of Boss by adding different growth factors as suggested by Anchan, Lin, Ferrari and Morshead in order to obtain a method for regulating the in vitro proliferation of a multipotent neural stem cell was within the ordinary skill in the art at the time the claimed invention was made. From the teachings of the references, it is

Art Unit: 1804

apparent that one of ordinary skill would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is prima facie obvious, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 9 and 10 are rejected under 35 U.S.C. § 103 as being unpatentable over Boss, Anchan, Lin, Morshead and Ferrari as applied to claims 1-8 above, and further in view of Gage. Claims 1-8 were rejected for reasons as stated above. Gage discloses transplantation of genetically modified cells to treat defects, disease or damage to the CNS. Gage further discloses that the cells are genetically modified to express a therapeutic gene of interest. It would have been obvious to one of ordinary skill to substitute the dopaminergic cell culture of Boss, Lin, Ferrari and Morshead for the genetically modified cells of Gage in view of the teachings of Gage that transplantation of donor cells from dopaminergic-rich areas have been shown to be effective in reversing the behavioral deficits. Regarding claims 9 and 10, the use of autologous cells is suggested by Gage, column 14, lines 39-46.

Accordingly, the modification of the method of Boss, Anchan, Lin, Ferrari and Morshead by using human cells derived from humans having a neurological disorder as suggested by Gage in order to obtain a method for regulating the in vitro proliferation of a multipotent neural stem cell was within the ordinary skill in the art at the time the claimed invention was made. From the teachings of the references, it is apparent that one of ordinary skill would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is prima facie obvious, as evidenced by the references, especially in the absence of evidence to the contrary.

Serial Number: 08/338,730

-7-

Art Unit: 1804

No claim is allowed.

Papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO FAX center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (30 November 15, 1989). The CM1 Fax Center number is (703) 308-4227.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Suzanne Ziska, Ph.D., whose telephone number is (703) 308-1217. In the event the examiner is not available, the examiner's supervisor, Ms. Jacqueline Stone, may be contacted at phone number (703) 308-3153.

Suzanne Ziska
Suzanne E. Ziska
PRIMARY EXAMINER
GROUP 1800